REMARKS

Claims 13-20 have been canceled as drawn to a non-elected invention. Claims 7-12 have been retained as methods of use of the compositions of claims 1 and 3 currently under examination which are subject to rejoinder pending allowance of claims 1 and 3 in accordance with *In Re:Ochiai.* See M.P.E.P. § 821.04. Claim 2 has been amended to delete "SEQ ID NO:5". Claim 4 has been amended to independent form and to recite " A vector comprising a cDNA encoding an amino acid sequence of SEQ ID NO:1". No new matter is added by any of these amendments and entry of the amendments is requested.

35 U.S.C. 101, Rejection of Claims 1-6

The Examiner has maintained the rejection of claims 1-6 under 35 U.S.C. § 101 for the reasons of record in paper No. 10. Specifically, the Examiner stated that the instant application does not disclose the biological role of this protein or its significance. The Examiner stated that the instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that TRP of the instant invention, which bears 85% identity to TIMM8b proteins, and which in turn bear homology to the proteins encoded by the gene associated with Mohr-Tranebjaerg syndrome, would also be associated with the Mohr-Tranebjaerg syndrome or with any or all of "various neurodegenerative and neuromuscular diseases involving defects in oxidative phosphorylation".

The Examiner also stated that with respect to Applicants asserted utility for the claimed polynucleotides in the diagnosis of breast, kidney and ovarian cancers, that the data of Table 2 supporting this assertion is "not definite" (emphasis added). The Examiner stated that it is not clear what is the difference in degree of expression of TRP in cancer/normal tissues, that some of the control results, for example, for ovary tumor seem absent. It is also not apparent, for example, for breast tumor and kidney tumor, how many samples were analyzed. If the results of Table 2 present the data obtained from a single sample, or less than three, for each of the cases---one of ordinary skill in the art would readily recognize that more statistical data is needed in order to make a sound scientific conclusion that TRP is clearly and specifically associated with these three cancers and therefore can be used as a marker for these diseases.

Applicants Response

Applicants disagree with the Examiner's allegations and submit that the Examiner has clearly failed to meet her burden of proof, as required by law, that one of skill in the art would doubt applicants assertions of utility for the claimed invention. The Examiner is reminded of the standard of the utility requirement as it is defined by law.

1. The Applicable Legal Standard

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression"

such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

Thus the Examiner is required by law to accept applicants assertions of utility unless the Examiner can provide evidence or sound scientific reasoning that a person of ordinary skill in the art would reasonably doubt the asserted utility, and the Examiner clearly has not done so. Applicants particularly object to the Examiner's allegation that the data presented in Table 2 is not "definite" in support of applicants assertion of utility of the claimed invention as a marker for various cancers. As noted above, there is no requirement in the law for "certainty" or "definiteness" in asserting a utility, applicant need only prove a "substantial likelihood" of utility. The Examiner merely alleges that a "single sample" or "less than three" would require "more statistical data in order to make a sound scientific conclusion". The Examiner offers no evidence of what constitutes sufficient evidence to support a

substantial likelihood of utility in this case. In addition, the specification describes the data in Table 2 as exemplary data showing libraries in which TRP was most abundantly expressed (i.e., overexpressed), not that they represented the only libraries in these categories that the transcript was found. The data clearly shows that the most abundant expression of TRP in breast, ovary and kidney libraries was found in cancerous tissues, and which in the case of both breast and kidney tumors were matched with normal tissue from the same donor in which expression was not found. While the ovarian tumor samples were not matched with normal tissue libraries from the same donor, it is clear from Table 1 that over 100 cDNA libraries were examined in the category of "Female Reproductive" (which includes ovary, cervical, and uterine tissues) and that no expression of TRP in normal ovarian tissue libraries was found. The Examiner does not dispute these findings and does not provide evidence or sound scientific reasoning why they would not support a substantial likelihood for the use of TRP in the diagnosis of breast, kidney, or ovarian cancer.

Applicants also disagree with the Examiner's allegation that there is not a "substantial likelihood" that TRP of the instant application would function in a manner similar to human TIMM8b based on the sequence homology given, and that even so, TIMM8b has no utility. As discussed in the previously response filed 7/11/02, specifically at p. 5, TRP differs from the human TIMM8b molecule only in the N-terminal 15 amino acids that most likely comprises a signal peptide, and is 100% identical over the remaining 82% of the molecule, including the $CX_3CX_{14}CX_3C$ motif of mitochondrial import proteins and which is characteristic of DDP/TIM family of proteins. See Jin et al. (1999) and Paschen et al. (2000). Jin et al specifically describe the human family of DDP/TIM-like proteins (including TIMM8b) as "candidate loci for autosomal recessive neurodegenerative disorders" (Abstract). In addition, the author describes the likely effects of defects in these mitochondrial genes as "mutations that may prove lethal" (bottom of p. 266, first column). Given the likely role of the DDP/TIM-like proteins in mitochondrial transport and their association with neurodegenerative disorders such as DDP, monitoring the expression of all of these proteins, including TRP, would be useful in detecting and diagnosing these disorders.

For all of the above reasons, applicants submit that both a well-established utility as well as a specific asserted utility has been established for the claimed invention, and therefore request withdrawal of the rejection of claims 1-6 under 35 U.S.C. § 101.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 1-6

The Examiner has maintained the rejection of claims 1-6 under 35 U.S.C. 112, first paragraph for the reasons of record in section 5 of Paper No.10. Applicants submit that for the reasons set forth above in the rejection of these claims under 35 U.S.C. § 101, a specific ans substantial utility has been established for the claimed invention, and therefore one skilled in the art would know how to use the claimed invention. Withdrawal of the rejection of these claims under 35 U.S.C. 112, first paragraph is therefore requested.

35 U.S.C. § 112, Second Paragraph, Rejection of Claims 2 and 6

The Examiner has rejected claims 2 and 6 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 2 is indefinite for recitation of "a fragment" of SEQ ID NO:5. Applicant submits that "SEQ ID NO:5 aligns over 321 base pairs of its sequence with the majority of the open reading frame of SEQ ID NO:2 and is clearly therefore a fragment of SEQ ID NO:5". Applicants have deleted SEQ ID NO:5 from claim 2.

The Examiner also stated that claim 6 is indefinite for recitation of "a protein" which is produced by the host cell of claim 5, and for missing a critical relationship because the claim is not limited to the host cell of claim 5 or the vector of claim 4. Claim 4 has been amended to independent form and to recite "a vector comprising a cDNA encoding SEQ ID NO:1".

Applicants believe that claims 2 and 6, as amended, are clear and definite, and therefore request withdrawal of the rejection of these claims under 35 U.S.C. § 112, second paragraph.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections Early notice to that effect is earnestly solicited. Applicants further request that, upon allowance of claims 1 and 3, that claims 7-12 be rejoined and examined as methods of use of the compositions of claims 1 and 3 and are subject to rejoinder pending allowance of claims 1 and 3 in accordance with *In Re:Ochiai.*

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of Record, below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**, as set forth in the enclosed fee transmittal letter.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: February 12, 2003 David G. Streeter

David G. Streeter, Ph.D.
Reg. No. 43,168
Direct Dial Telephone: (650) 845-5741

3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 13-20 have been canceled.

Claim) 2 and 4 have been amended as follows:

2. (Once Amended) An isolated cDNA comprising a nucleic acid sequence selected from:

a) SEQ ID NO:2 or the complement thereof;

b) a fragment of SEQ ID NO:2 selected from SEQ ID NOs:3-4[5] or the complement thereof; and

c) a variant of SEQ ID NO:2 selected from SEQ ID NOs:6-11 or the complement thereof.

4. (Once Amended) A vector comprising a [the] cDNA encoding an amino acid sequence of SEQ ID NO:1 [of claim 1].